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13. ABSTRACT

Increased susceptibility to ornithosis virus, administered by aerosol, was observed in white mice pretreated with x-rays. A shortening of the incubation period, observed in the irradiated, infected animals, depends on x-ray dose, virus dose and time interval between irradiation and infection. Ornithosis virus is retained longer and reaches higher titres in the lungs, liver and spleen of irradiated animals.

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EFFECT OF PRELIMINARY X-IRRADIATION ON THE SUSCEPTIBILITY OF WHITE MICE TO ORNITHOSIS VIRUS UPON INFECTION WITH AN AEROSOL OF THE VIRUS

There is only one report in the literature on the question of experimental study of aerosol infection in previously irradiated animals [5]. The office has carried out irradiation of white mice with x-rays induces of 50-750r, and after three days infected them with an aerosol of grippe virus (strain PR-8). As a result an interesting fact was noted: upon infection with an aerosol of virus adapted to pulmonary tissue of white mice, morbidity was identical among irradiated and controlled animals, but more intensive infection of the lung tissue was observed in the irradiated mice. Unadapted virus (allantois culture) also caused more pronounced disease in irradiated animals, and more intensive lung infection in comparison with controlled. Thus, preliminary irradiation of animals undoubtedly to a certain extent increased their sensitivity to aerosol infection by grippe virus.

The purpose of our work was to show how the susceptibility of initially irradiated white mice changes toward ornithosis virus upon infection with an aerosol of the virus.

1. Material and Methods

Experiments are carried out in white mice weighing 7-9g. Conditions of irradiation: RUM-11 apparat s, current intensity 15 ma, voltage 150 kv, filter 3 mm Al, focal distance 75 cm, irradiation dose 22.5 r/min.

Mice were irradiated with single, total, doses of 200, 300, 400, 500, 700 r. Mice were infected in a IVK-1 chamber [2] on the 2nd, 5th, 10th, and 19th day after irradiation. Ornithosis virus, strain B (isolated from a sick person in 1948), adapted to pulmonary tissue of white mice was used in the experiment. The virus titre at the time of the experiments varied negligibly - in the range of 6.5-7.5 LD_{50} (upon intracerebral titration). The lung suspension from infected mice was prepared on Martin's broth pH 7.4. Dilutions of virus from 10^{-1} to 10^{-6} we used in the experiments.

2. Results

In the first series of experiments we attempted to show whether the susceptibility of white mice to ornithosis virus depended on the dose of x-rays and whether the susceptibility changes upon infection of the mice at different times after irradiation. Through infection of the mice, 9ml of virus-containing lung suspension at dilutions of 10^{-3} or 10^{-4}, which corresponded to 1,000 LD_{50} (upon intracerebral titration), were poured into an atomizer, installed in the chamber.

The virus containing suspension was sprayed at a rate of 14-14.5 l per minute for 17 minutes; during that time 3-3.5 ml of suspension was sprayed in 238-246 l of air. The time of contact of the mice with the received aerosol was 60 minutes. Knowing the respiratory volume of mouse lungs (1.1 ml per g of body weight), the weight of the animal (8 g), the time of contact with the virus (60 minutes), the virus concentration (0.000012 g/ml), one may calculate the amount of suspension absorbed by each animal (1.1 ml/g × 8 g × 60 mins. × 0.000012 g/ml). This is 0.0063336 g, which is approximately 8 times less than intranasal infection. Mice received x irradiation in doses of 200, 300, 400, 500, 700 r and were infected with an aerosol virus on the 2nd, 5th, 10th, 19th day after irradiation.

In Table 1 the average data of three experiments are presented.

Table 1. Effect of preliminary irradiation with various doses of x-rays on the susceptibility of white mice to ornithosis virus upon infection at various times after irradiation

irradiation dose (in r)[1]	% irradiated white mice destroyed	day after irradiation: 2nd		5th		10th		19th	
		deaths	incubation period	deaths	incubation period	deaths	incubation period	deaths	incubation period
700	80	100	8,5	100	9,4	100	4,2	100	4,5
500	60	80	8,5	100	12,5	100	13,6	100	12,2
400	58,3	92,5	11,25	82,5	11,8	92	11,3	86,4	14,9
300	30	65	11,3	71,2	12,2	71,7	12,3	84,5	14,3
200	3	70	19,1	90	21,3	95	18,1	83,3	19,5
Control (non-irradiated)		45	17,1	51,4	18,3	63	16,2	74	18,8

From Table 1 it can be seen that upon infection of mice at various times after irradiation, death of irradiated animals increases, but very slightly. If one considers the incubation period, it can be seen that in the irradiated animals it is significantly shorter than in controlled, while if an increase in the dose of x-rays a shortening of the incubation period occurs. Animals receiving a dose of 200 r are the only exception. Results of the study of susceptibility of animals upon infection at various times after irradiation have shown that in proportion to the elimination of the period of infection, the duration of the incubation period increases remaining constantly lower than the control.

Each experiment was performed on 580 mice, with about 20 mice per group, in the control radiation disease also remained about 20 mice irradiated with various doses of x-rays. The virus retained its biological activity in the course of the experiment.

In the second series of experiments virus titration was carried out in mice irradiated with various doses of x-rays on the 2nd and 19th day after irradiation, and in mice of a control group. Conditions of the work chamber was the same as those in the preceeding series of experiments. In these experiments also we did not succeed in obtaining significant difference in death between irradiated and controlled animals. But here a difference in the incubation period was also noted: the higher the dose of radiation in virus, the shorter the incubation period. This dependance was observed both on the 2nd and the 19th day after irradiation (Table 2).

In the following experiments, studying pathogenesis of infection, we determined the accumulation of virus in the organs of mice irradiated with a dose of 300 r and infected with 1,000 LD_{50} of virus on the 2nd day after irradiation. Up to 5 irradiated and up to 5 control mice were dissected on the 7th, 14th, 24th, 30th, 44th, 60th, and 90th day after infection. A 10% suspension of the lungs, liver and spleen, blood, kidneys was prepared in Martin's broth and intracerebral passages with this material were carried out in mice. The results of this experiment are presented in Table 3.

As can be seen from Table 3, viruses were detected in the lung from the 7th to the 90th day after infection both in irradiated and control animals. On the 7th and 14th day after infection the virus titre in the lungs of irradiated and controlled animals were identical. The virus titre was higher in the lungs of irradiated animals at a later period. On the 30th day after infection the virus titre in irradiated animals reached log LD_{50} 5.67, in the lungs of control mice - log LD_{50}-1. On the 90th day in the lungs of irradiated mice the virus was detected at a titre of log LD_{50}-1.67, and in the lungs of control mice the log LD_{50} was 1. In the liver and spleen the virus was detected from the 14th to the 90th day. In the kidneys the virus was not detected.

Table 2. Effect of irradiation on susceptibility of mice to ornithosis virus upon infection with various doses of virus

irradiation dose (in r)	infection on 2nd day after irradiation upon dilution of virus				infection on 19th day after irradiation after dilution of virus			
	10^{-1}	10^{-2}	10^{-4}	10^{-6}	10^{-1}	10^{-2}	10^{-4}	10^{-6}
	incubation period							
700	6	5,6	8,5	8,6	—	—	—	—
500	7,8	7,4	8,5	15,4	6,8	8	17	17
300	7,6	10,5	12,6	21,7	6,9	8,4	15,3	17
200	10,5	15,7	19,1	24,2	8	9,6	19	32,2
control (non-irradiated)	11,8	14,5	20,7	23,4	8,5	9,7	21,4	24

Note: — experiments were not carried out.

Table 3. Dynamics of distribution of virus in organs of animals infected on the 2nd day after irradiation

organ	day after irradiation													
	7th		14th		24th		30th		44th		60th		90th	
	i	c	i	c	i	c	i	c	i	c	i	c	i	c
lung	3,3	3,3	3	3	—	—	5,67	1	—	—	—	—	1,67	1
blood	—	—	2	—	—	—	—	—	—	—	—	—	—	—
liver & spleen	—	—	3	4,2	—	—	1,67	—	—	—	—	—	5,5	1
kidney	—	—	—	—	—	—	—	—	—	—	—	—	—	—

Note: - During primary infection of white mice virus was not isolated; i - irradiated animals; c - controls.

Our results correspond with data presented in works by Beutlar and Gezon.

Upon intranasal infection with grippe virus, O.P. Peterson and I.A. Kozlova obtained results indicating a significant increase in susceptibility of animals to infection after infection on the 2nd to 6th day after irradiation [1]. Analogous data was also obtained by A.A. Smorodintsev [3]. It is possible that in the given case the higher pathogenecity is explained by the method of introduction of

virus with a character of the infection, during which the incubation period was shorter.

O.P. Peterson, O.N. Berezina, I.A. Kozlova and Ye.I. Sklyanskaya have shown that during virus infection having a long incubation period, the susceptibility of irradiated animals essentially does not change [2, 3]. The infection of animals with doses of an aerosol of ornithosis virus, during which 50 to 70% death was observed in the control, was accompanied by a long incubation period. It is possible that this can be explained by the insignificant increase which we observed in deaths of irradiated and infected animals.

3. Conclusions

1. The irradiation of white mice prior to infection with an aerosol of ornithosis virus increased their susceptibility to this virus - a shortening of the incubation period by several days and some increase in animal deaths.

2. In lungs, liver and spleen of irradiated animals the viruses retained for a longer time and a higher titres.

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